

**WEST**

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L2: Entry 7 of 16

File: USPT

Jun 1, 1999

US-PAT-NO: 5908777

DOCUMENT-IDENTIFIER: US 5908777 A

TITLE: Lipidic vector for nucleic acid delivery

DATE-ISSUED: June 1, 1999

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Lee; Robert J.	Pittsburgh	PA		
Huang; Leaf	Wexford	PA		

US-CL-CURRENT: 435/320.1; 264/4.1, 424/450, 424/93.21, 435/325, 435/458, 435/69.1,  
514/44

## CLAIMS:

What is claimed is:

1. A method for creating a lipidic vector for nucleic acid delivery, comprising the steps of

(A) providing a nucleic acid with a polycation to condense said nucleic acid in a nucleic acid/polycation complex; and

(B) combining an anionic lipidic preparation with said nucleic acid/polycation complex to form said lipidic vector.

2. A method according to claim 1, wherein a ligand is added to said lipidic vector (i) by covalently bonding said ligand to said anionic lipidic preparation or to said polycation, or (ii) by mixing said ligand with said anionic lipidic preparation or said nucleic acid/polycation complex.

3. A method according to claim 2, wherein said ligand is at least one selected from the group consisting of a tissue-specific ligand, a cellular receptor-targeting ligand, a fusogenic peptide, and a nucleus-targeting peptide.

4. A method according to claim 1, wherein said polycation is selected from the group consisting of (1) a non-monovalent cation; (2) a cationic polymer; and (3) a cationic detergent.

5. A method according to claim 1, wherein said polycation is an acid.

6. A method according to claim 1, further comprising a step of adding a ligand or a combination of ligands selected from the group consisting of (a) a cellular receptor-targeting ligand; (2) a fusogenic ligand; (3) a nucleus-targeting ligand; and (4) a combination of said ligands.

7. A lipidic vector for nucleic acid delivery, said vector being the product of a method according to claim 1.

8. A method according to claim 1, wherein said polycation is selected from the group consisting of: polylysine, protamine, DEAE-dextran, cationized albumin,

polybrene, spermine, polyornithine, a histone, a cascade amidoamine dendritic polymer, gramicidin S cyclic peptide, and spermidine.

9. The method according to claim 4, wherein said non-monovalent cation is selected from the group consisting of  $\text{Ca}^{+2}$ ,  $\text{Mg}^{+2}$ ,  $\text{Mn}^{+2}$ ,  $\text{Al}^{+3}$ , spermine and spermidine.

10. The method according to claim 4, wherein said cationic polymer is selected from the group consisting of polylysine, DEAE-dextran, protamine, polybrene, and a cationized protein.

11. The method according to claim 4, wherein said cationic detergent is selected from the group consisting of DC-chol and cetyltrimethylammonium bromide (CTAB).

## WEST Search History

DATE: Thursday, June 26, 2003

Set Name Query  
side by side

Hit Count Set Name  
result set

*DB=USPT,JPAB,EPAB,DWPI,TDBD; PLUR=YES; OP=OR*

L4	(liposome\$) same (free adj1 fatty)	41	L4
L3	(cationic adj1 liposome\$) same (free adj1 fatty)	0	L3
L2	L1 and ((424/450)!.CCLS. )	16	L2
L1	(cationic adj1 liposome\$) same (fatty adj1 acid)	76	L1

END OF SEARCH HISTORY

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L4: Entry 3 of 41

File: USPT

Oct 15, 2002

DOCUMENT-IDENTIFIER: US 6465188 B1  
TITLE: Nucleic acid ligand complexes

Detailed Description Text (37):

A Nucleic Acid Ligand or ligands in association with a Lipophilic Compound or Non-Immunogenic, High Molecular Weight Compound may enhance the intracellular delivery of the Nucleic Acid Ligand(s) over non-associated Nucleic Acid Ligand(s). The efficiency of delivery of the Complex to cells may be optimized by using lipid formulations and conditions known to enhance fusion of Liposomes with cellular membranes. For example, certain negatively charged lipids such as phosphatidylglycerol and phosphatidylserine promote fusion, especially in the presence of other fusogens (e.g., multivalent cations like  $\text{Ca}^{2+}$ , free fatty acids, viral fusion proteins, short chain PEG, lysolecithin, detergents and surfactants). Phosphatidylethanolamine may also be included in the Liposome formulation to increase membrane fusion and, concomitantly, enhance cellular delivery. In addition, free fatty acids and derivatives thereof, containing, for example, carboxylate moieties, may be used to prepare pH-sensitive Liposomes which are negatively charged at higher pH and neutral or protonated at lower pH. Such pH-sensitive Liposomes are known to possess a greater tendency to fuse.

## WEST Search History

DATE: Thursday, June 26, 2003

Set Name Query  
side by side

Hit Count Set Name  
result set

*DB=USPT,JPAB,EPAB,DWPI,TDBD; PLUR=YES; OP=OR*

L4	\$trimethylammoniumpropane same (fatty adj1 acid\$)	1	L4
L3	L2 and fatty	11	L3
L2	\$trimethylammoniumpropane	18	L2
L1	\$dimethylammoniumpropane	5	L1

END OF SEARCH HISTORY

**WEST****End of Result Set**☐

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L1: Entry 5 of 5

File: USPT

Sep 15, 1998

DOCUMENT-IDENTIFIER: US 5807572 A

TITLE: Multivesicular liposomes having a biologically active substance encapsulated therein in the presence of a hydrochloride

## CLAIMS:

12. The process according to claim 1 or 2 wherein, the lipid component further comprises stearylamine, or diacyl dimethylammoniumpropane, or diacyl trimethylammoniumpropane.

**WEST**[Generate Collection](#)[Print](#)**Search Results - Record(s) 1 through 5 of 5 returned.**☐ 1. Document ID: US 6562371 B1

L1: Entry 1 of 5

File: USPT

May 13, 2003

US-PAT-NO: 6562371

DOCUMENT-IDENTIFIER: US 6562371 B1

TITLE: Liposomes

DATE-ISSUED: May 13, 2003

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kawahara; Kazuo	Kanagawa			JP
Ushijima; Hideto	Kanagawa			JP
Uchiyama; Hideki	Kanagawa			JP
Kimura; Junji	Kanagawa			JP

US-CL-CURRENT: 424/450; 424/1.21, 424/9.321, 424/9.51, 428/402.2

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWIC
Draw Desc	Image										

☐ 2. Document ID: US 6287591 B1

L1: Entry 2 of 5

File: USPT

Sep 11, 2001 ,

US-PAT-NO: 6287591

DOCUMENT-IDENTIFIER: US 6287591 B1

TITLE: Charged therapeutic agents encapsulated in lipid particles containing four lipid components

DATE-ISSUED: September 11, 2001

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Semple; Sean C.	Vancouver			CA
Klimuk; Sandra K.	N. Vancouver			CA
Harasym; Troy	Vancouver			CA
Hope; Michael J.	Vancouver			CA
Ansell; Steven M.	Vancouver			CA
Cullis; Pieter	Vancouver			CA
Scherrer; Peter	Vancouver			CA
Debeyer; Dan	Vancouver			CA

US-CL-CURRENT: 424/450; 428/402.2, 435/177, 435/458, 514/44, 536/22.1

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KMIC
Draw Desc	Image										

☐ 3. Document ID: US 6258378 B1

L1: Entry 3 of 5

File: USPT

Jul 10, 2001

US-PAT-NO: 6258378

DOCUMENT-IDENTIFIER: US 6258378 B1

TITLE: Delivery of biologically active substance to target sites in the body of patients

DATE-ISSUED: July 10, 2001

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Schneider; Michel	Troinex			CH
Yan; Feng	Carouge			CH
Hiver; Agnes	Clarafond			FR

US-CL-CURRENT: 424/450; 424/1.21, 424/812, 424/9.321, 424/9.51, 436/829

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KMIC
Draw Desc	Image									

☐ 4. Document ID: US 6071534 A

L1: Entry 4 of 5

File: USPT

Jun 6, 2000

US-PAT-NO: 6071534

DOCUMENT-IDENTIFIER: US 6071534 A

TITLE: Multivesicular liposomes with controlled release of active agents encapsulated in the presence of a hydrochloride

DATE-ISSUED: June 6, 2000

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kim; Sinil	Solana Beach	CA		
Howell; Stephen B.	Del Mar	CA		

US-CL-CURRENT: 424/450; 264/4.1, 264/4.3, 264/4.6, 436/829

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KMIC
Draw Desc	Image									

☐ 5. Document ID: US 5807572 A



· L1: Entry 5 of 5

File: USPT

Sep 15, 1998

US-PAT-NO: 5807572

DOCUMENT-IDENTIFIER: US 5807572 A

TITLE: Multivesicular liposomes having a biologically active substance encapsulated therein in the presence of a hydrochloride

DATE-ISSUED: September 15, 1998

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kim; Sinil	Solana Beach	CA		
Howell; Stephen B.	Del Mar	CA		

US-CL-CURRENT: 424/450; 264/4.1, 264/4.3

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KWIC
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Terms	Documents
\$dimethylammoniumpropane	5

**Display Format:**

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[Change Format](#)[Previous Page](#)[Next Page](#)

**WEST**[Generate Collection](#)[Print](#)**Search Results - Record(s) 1 through 18 of 18 returned.**☐ 1. Document ID: US 6562371 B1

L2: Entry 1 of 18

File: USPT

May 13, 2003

US-PAT-NO: 6562371

DOCUMENT-IDENTIFIER: US 6562371 B1

TITLE: Liposomes

DATE-ISSUED: May 13, 2003

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kawahara; Kazuo	Kanagawa			JP
Ushijima; Hideto	Kanagawa			JP
Uchiyama; Hideki	Kanagawa			JP
Kimura; Junji	Kanagawa			JP

US-CL-CURRENT: [424/450](#); [424/1.21](#), [424/9.321](#), [424/9.51](#), [428/402.2](#)

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KWIC
Draw Desc	Image									

☐ 2. Document ID: US 6548287 B1

L2: Entry 2 of 18

File: USPT

Apr 15, 2003

US-PAT-NO: 6548287

DOCUMENT-IDENTIFIER: US 6548287 B1

TITLE: Non-pyrogenic bacterial strains and use of the same

DATE-ISSUED: April 15, 2003

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Powell; Robert J.	Baltimore	MD		
Hone; David M.	Ellicott City	MD		

US-CL-CURRENT: [435/243](#); [424/234.1](#), [424/241.1](#), [424/245.1](#), [424/249.1](#), [424/253.1](#), [424/258.1](#), [424/260.1](#), [424/261.1](#), [435/170](#), [435/252.3](#), [435/69.3](#)

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KWIC
Draw Desc	Image									

☐ 3. Document ID: US 6306432 B1

L2: Entry 3 of 18

File: USPT

Oct 23, 2001

US-PAT-NO: 6306432

DOCUMENT-IDENTIFIER: US 6306432 B1

TITLE: High and low load formulations of IGF-I in multivesicular liposomes

DATE-ISSUED: October 23, 2001

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Shirley; Bret	Concord	CA		
Hora; Maninder	Danville	CA		
Ye; Qiang	San Diego	CA		
Katre; Nandini	Solana Beach	CA		
Asherman; John	San Diego	CA		

US-CL-CURRENT: 424/450; 264/4.1, 264/4.3, 514/21, 514/3

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KWIC
Draw Desc	Image									

☐ 4. Document ID: US 6258378 B1

L2: Entry 4 of 18

File: USPT

Jul 10, 2001

US-PAT-NO: 6258378

DOCUMENT-IDENTIFIER: US 6258378 B1

TITLE: Delivery of biologically active substance to target sites in the body of patients

DATE-ISSUED: July 10, 2001

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Schneider; Michel	Troinex			CH
Yan; Feng	Carouge			CH
Hiver; Agnes	Clarafond			FR

US-CL-CURRENT: 424/450; 424/1.21, 424/812, 424/9.321, 424/9.51, 436/829

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KWIC
Draw Desc	Image									

☐ 5. Document ID: US 6241999 B1

L2: Entry 5 of 18

File: USPT

Jun 5, 2001

US-PAT-NO: 6241999

DOCUMENT-IDENTIFIER: US 6241999 B1

**\*\* See image for Certificate of Correction \*\***

TITLE: Method for producing liposomes with increased percent of compound encapsulated

DATE-ISSUED: June 5, 2001

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ye; Qiang	San Diego	CA		
Sankaram; Mantripragada Bhima	San Diego	CA		

US-CL-CURRENT: 424/450; 264/4.1, 264/4.3, 264/4.6

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KVMC
Draw Desc	Image									

☐ 6. Document ID: US 6193998 B1

L2: Entry 6 of 18

File: USPT

Feb 27, 2001

US-PAT-NO: 6193998

DOCUMENT-IDENTIFIER: US 6193998 B1

**\*\* See image for Certificate of Correction \*\***

TITLE: Method for producing liposomes with increased percent of compound encapsulated

DATE-ISSUED: February 27, 2001

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ye; Qiang	San Diego	CA		
Sankaram; Mantripragada Bhima	San Diego	CA		

US-CL-CURRENT: 424/450; 264/4.1, 264/4.3, 424/1.21, 424/417, 424/9.321, 424/9.51, 424/94.3

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KVMC
Draw Desc	Image									

☐ 7. Document ID: US 6171613 B1

L2: Entry 7 of 18

File: USPT

Jan 9, 2001

US-PAT-NO: 6171613

DOCUMENT-IDENTIFIER: US 6171613 B1

TITLE: Method for producing liposomes with increased percent of compound encapsulated

DATE-ISSUED: January 9, 2001

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ye; Qiang	San Diego	CA		
Sankaram; Mantripragada Bhima	San Diego	CA		

US-CL-CURRENT: 424/450; 264/4.1, 264/4.3, 264/4.6, 424/1.21, 424/417, 424/9.34,  
424/9.51, 436/829

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
Draw Desc	Image								

KMC

☐ 8. Document ID: US 6106858 A

L2: Entry 8 of 18

File: USPT

Aug 22, 2000

US-PAT-NO: 6106858

DOCUMENT-IDENTIFIER: US 6106858 A

**\*\* See image for Certificate of Correction \*\***

TITLE: Modulation of drug loading in multivesicular liposomes

DATE-ISSUED: August 22, 2000

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ye; Qiang	San Diego	CA		
Katre; Nandini	Solana Beach	CA		
Sankaram; Mantripragada	San Diego	CA		

US-CL-CURRENT: 424/450; 264/4.1, 264/4.3

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
Draw Desc	Image								

KMC

☐ 9. Document ID: US 6071534 A

L2: Entry 9 of 18

File: USPT

Jun 6, 2000

US-PAT-NO: 6071534

DOCUMENT-IDENTIFIER: US 6071534 A

TITLE: Multivesicular liposomes with controlled release of active agents encapsulated in the presence of a hydrochloride

DATE-ISSUED: June 6, 2000

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kim; Sinil	Solana Beach	CA		
Howell; Stephen B.	Del Mar	CA		

US-CL-CURRENT: 424/450; 264/4.1, 264/4.3, 264/4.6, 436/829

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
Draw Desc	Image								

KMC

☐ 10. Document ID: US 6011020 A

L2: Entry 10 of 18

File: USPT

Jan 4, 2000

US-PAT-NO: 6011020

DOCUMENT-IDENTIFIER: US 6011020 A

TITLE: Nucleic acid ligand complexes

DATE-ISSUED: January 4, 2000

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Gold; Larry	Boulder	CO		
Schmidt; Paul G.	San Marino	CA		
Janjic; Nebojsa	Boulder	CO		

US-CL-CURRENT: 514/44; 424/1.21, 424/1.73, 424/450, 435/6, 536/22.1, 536/23.1, 536/24.3, 536/24.31

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KWIC
Draw Desc	Image									

☐ 11. Document ID: US 5997899 A

L2: Entry 11 of 18

File: USPT

Dec 7, 1999

US-PAT-NO: 5997899

DOCUMENT-IDENTIFIER: US 5997899 A

TITLE: Method for producing liposomes with increased percent of compound encapsulated

DATE-ISSUED: December 7, 1999

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ye; Qiang	San Diego	CA		
Sankaram; Mantripragada Bhima	San Diego	CA		

US-CL-CURRENT: 424/450

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KWIC
Draw Desc	Image									

☐ 12. Document ID: US 5997881 A

L2: Entry 12 of 18

File: USPT

Dec 7, 1999

US-PAT-NO: 5997881

DOCUMENT-IDENTIFIER: US 5997881 A

\*\* See image for Certificate of Correction \*\*

TITLE: Method of making non-pyrogenic lipopolysaccharide or A

DATE-ISSUED: December 7, 1999

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Powell; Robert J.	Baltimore	MD		
Hone; David M.	Ellicott City	MD		

US-CL-CURRENT: 424/234.1; 424/240.1, 424/241.1, 424/245.1, 424/249.1, 424/252.1,  
424/253.1, 424/258.1, 424/259.1, 424/260.1, 424/261.1, 435/170, 435/243

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KMIC
Draw Desc	Image									

☐ 13. Document ID: US 5962016 A

L2: Entry 13 of 18

File: USPT

Oct 5, 1999

US-PAT-NO: 5962016

DOCUMENT-IDENTIFIER: US 5962016 A

TITLE: Multivesicular liposomes utilizing neutral lipids to modify in vivo release

DATE-ISSUED: October 5, 1999

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Willis; Randall C.	Solana Beach	CA		

US-CL-CURRENT: 424/450

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KMIC
Draw Desc	Image									

☐ 14. Document ID: US 5891467 A

L2: Entry 14 of 18

File: USPT

Apr 6, 1999

US-PAT-NO: 5891467

DOCUMENT-IDENTIFIER: US 5891467 A

**\*\* See image for Certificate of Correction \*\***

TITLE: Method for utilizing neutral lipids to modify in vivo release from multivesicular liposomes

DATE-ISSUED: April 6, 1999

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Willis; Randall C.	Solana Beach	CA		

US-CL-CURRENT: 424/450; 424/417, 436/829

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
Draw Desc	Image								

KMIC

☐ 15. Document ID: US 5807572 A

L2: Entry 15 of 18

File: USPT

Sep 15, 1998

US-PAT-NO: 5807572

DOCUMENT-IDENTIFIER: US 5807572 A

TITLE: Multivesicular liposomes having a biologically active substance encapsulated therein in the presence of a hydrochloride

DATE-ISSUED: September 15, 1998

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kim; Sinil	Solana Beach	CA		
Howell; Stephen B.	Del Mar	CA		

US-CL-CURRENT: 424/450; 264/4.1, 264/4.3

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
Draw Desc	Image								

KMIC

☐ 16. Document ID: US 5795870 A

L2: Entry 16 of 18

File: USPT

Aug 18, 1998

US-PAT-NO: 5795870

DOCUMENT-IDENTIFIER: US 5795870 A

TITLE: Compositions and methods for cell transformation

DATE-ISSUED: August 18, 1998

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kahne; Suzanne Walker	Princeton	NJ		

US-CL-CURRENT: 514/26; 514/169, 514/171, 536/5

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
Draw Desc	Image								

KMIC

☐ 17. Document ID: US 5780444 A

L2: Entry 17 of 18

File: USPT

Jul 14, 1998

US-PAT-NO: 5780444

DOCUMENT-IDENTIFIER: US 5780444 A



TITLE: Compositions and methods for cell transformation

DATE-ISSUED: July 14, 1998

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kahne; Suzanne Walker	Princeton	NJ		

US-CL-CURRENT: 514/26; 514/169, 514/170, 514/178, 514/182, 536/5, 930/10

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KMIC
Draw Desc	Image									

☐ 18. Document ID: US 5723147 A

L2: Entry 18 of 18

File: USPT

Mar 3, 1998

US-PAT-NO: 5723147

DOCUMENT-IDENTIFIER: US 5723147 A

**\*\* See image for Certificate of Correction \*\***

TITLE: Multivesicular liposomes having a biologically active substance encapsulated therein in the presence of a hydrochloride

DATE-ISSUED: March 3, 1998

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kim; Sinil	Solana Beach	CA		
Howell; Stephen B.	Del Mar	CA		

US-CL-CURRENT: 424/450

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KMIC
Draw Desc	Image									

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Terms	Documents
Strimethylammoniumpropane	18

Display Format:  Change Format

[Previous Page](#)

[Next Page](#)

**WEST**

Generate Collection

Print

L3: Entry 6 of 11

File: USPT

Jan 4, 2000

DOCUMENT-IDENTIFIER: US 6011020 A

TITLE: Nucleic acid ligand complexes

Brief Summary Text (15):

Liposomes are a subset of these bilayer vesicles and are comprised principally of phospholipid molecules that contain two hydrophobic tails consisting of fatty acid chains. Upon exposure to water, these molecules spontaneously align to form spherical, bilayer membranes with the lipophilic ends of the molecules in each layer associated in the center of the membrane and the opposing polar ends forming the respective inner and outer surface of the bilayer membrane(s). Thus, each side of the membrane presents a hydrophilic surface while the interior of the membrane comprises a lipophilic medium. These membranes may be arranged in a series of concentric, spherical membranes separated by thin strata of water, in a manner not dissimilar to the layers of an onion, around an internal aqueous space. These multilamellar vesicles (MLV) can be converted into small or Unilamellar Vesicles (UV), with the application of a shearing force.

Detailed Description Text (13):

"Liposomes" are a subset of bilayer vesicles and are comprised principally of phospholipid molecules which contain two hydrophobic tails consisting of long fatty acid chains. Upon exposure to water, these molecules spontaneously align to form a bilayer membrane with the lipophilic ends of the molecules in each layer associated in the center of the membrane and the opposing polar ends forming the respective inner and outer surface of the bilayer membrane. Thus, each side of the membrane presents a hydrophilic surface while the interior of the membrane comprises a lipophilic medium. These membranes when formed are generally arranged in a system of concentric closed membranes separated by interlamellar aqueous phases, in a manner not dissimilar to the layers of an onion, around an internal aqueous space. These multilamellar vesicles (MLV) can be converted into small or unilamellar vesicles (UV), with the application of a shearing force.

Detailed Description Text (38):

A Nucleic Acid Ligand or ligands in association with a Lipophilic Compound or Non-Immunogenic, High Molecular Weight Compound may enhance the intracellular delivery of the Nucleic Acid Ligand(s) over non-associated Nucleic Acid Ligand(s). The efficiency of delivery of the Complex to cells may be optimized by using lipid formulations and conditions known to enhance fusion of Liposomes with cellular membranes. For example, certain negatively charged lipids such as phosphatidylglycerol and phosphatidylserine promote fusion, especially in the presence of other fusogens (e.g., multivalent cations like Ca.sup.2+, free fatty acids, viral fusion proteins, short chain PEG, lysolecithin, detergents and surfactants). Phosphatidylethanolamine may also be included in the Liposome formulation to increase membrane fusion and, concomitantly, enhance cellular delivery. In addition, free fatty acids and derivatives thereof, containing, for example, carboxylate moieties, may be used to prepare pH-sensitive Liposomes which are negatively charged at higher pH and neutral or protonated at lower pH. Such pH-sensitive Liposomes are known to possess a greater tendency to fuse.

Detailed Description Paragraph Table (1):

## TABLE 1

Summary of Liposome NX232 Preparations - Lipid compositions and mole percentage of NX232 Compound.sup.a M.W. A B C D E F G H

```

fractions: DSPC 790.15 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 Chol 386.7 1.0 1.0 1.0 1.0 1.0
1.0 1.0 1.0 DOTAP 698.55 0.0 0.0 0.0 0.0 0.0 0.0012 0.003 0.006 0.012 NX232 12,424.1
0.0003 0.0008 0.0015 0.003 0.0003 0.0008 0.0015 0.003 (NX232 mole-%) 0.01 0.025 0.05
0.1 0.01 0.025 0.05 0.1 Weight Ratios: DSPC 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 Chol
0.2447 0.2447 0.2447 0.2447 0.2447 0.2447 0.2447 0.2447 DOTAP 0.0 0.0 0.0 0.0 0.0005
0.0013 0.0027 0.0053 NX232 0.0024 0.0059 0.0118 0.0236 0.0024 0.0059 0.0118 0.0236
Amounts per ml.sup.b : DSPC 20.0 20.0 20.0 20.0 20.0 20.0 20.0 20.0 Chol 4.894 4.894
4.894 4.894 4.894 4.894 4.894 DOTAP 0.0 0.0 0.0 0.0 0.011 0.027 0.053 0.106
NX232 0.047 0.118 0.236 0.472 0.047 0.118 0.236 0.472

```

DSPC = distearoylphosphaatidylcholine; Chol = cholesterol; DOTAP =  
1,2dioleoyl-3-trimethylammoniumpropane. .sup.b final total concentration for all  
 components = 25 mg/ml.

**WEST**

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☐ 1. Document ID: US 6258378 B1

L4: Entry 1 of 1

File: USPT

Jul 10, 2001

US-PAT-NO: 6258378

DOCUMENT-IDENTIFIER: US 6258378 B1

TITLE: Delivery of biologically active substance to target sites in the body of patients

DATE-ISSUED: July 10, 2001

**INVENTOR-INFORMATION:**

NAME	CITY	STATE	ZIP CODE	COUNTRY
Schneider; Michel	Troinex			CH
Yan; Feng	Carouge			CH
Hiver; Agnes	Clarafond			FR

US-CL-CURRENT: 424/450; 424/1.21, 424/812, 424/9.321, 424/9.51, 436/829

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KWIC
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Terms	Documents
\$trimethylammoniumpropane same (fatty adj1 acid\$)	1

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